Remarks

Claims 1, 6-8, and 51-62 are pending in the subject application. By this Amendment, Applicants have amended claims 1, 6-8, 54-58, and 62. Support for the amendments can be found throughout the subject specification and in the claims as originally filed (see, for example, page 17, lines 1-4). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 6-8, and 51-62 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Applicants gratefully acknowledge the Examiner's withdrawal of the objections to the specification and the claims and the rejections under 35 U.S.C. §§ 101, 112, second paragraph, 102(e), and 102(f). Applicants also wish to draw the Examiner's attention to the Office Actions issued in U.S. Patent Application Serial No. 10/872,859 (a related application also under examination by the Examiner). Although electronic copies of the Office Actions in the '859 application are available via the Patent Application Information Retrieval system (PAIR), copies of the Office Actions are attached hereto for the Examiner's convenience. Examination in another application in this family (U.S. Patent Application Serial No. 10/558,800, now docketed to the Examiner) has not, as of this date, begun.

Claims 1, 6-8, and 51-62 are rejected under 35 U.S.C. § 112, first paragraph, as nonenabled for fragments, "functional equivalents", or polypeptides having only 90% identity to the polypeptide of SEQ ID NO: 2. The Office Action notes that while the effects of some mutations are known to those skilled in the art, mutations of other residues may or may not be as predictable. Even if the family of IFN-γ proteins is well-known, the polypeptide of the instant invention is not IFN-γ, but rather an "IFN-γ-like" protein with a different primary amino acid sequence. One of ordinary skill in the art would not necessarily be able to predict the effect of mutating all possible amino acid residues required to create a protein with 90% identity to the sequence of SEQ ID NO: 2, and would require further, undue experimentation in order to do so. Therefore, the Office Action indicates that while the specification is enabled for an isolated polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2, it is not enabled for the full breadth of the claims regarding polypeptides with only 90% identity to SEQ ID NO: 2, or fragments of polypeptides having only 90% identity to

SEQ ID NO: 2. Applicants respectfully assert that the claims are enabled by the subject specification.

As noted in the as-filed specification, polypeptides of SEQ ID NO: 2 that contained additional amino acids appended to the polypeptide retained biological activity. In Example 6, INSP037 (SEQ ID NO: 2) polypeptides containing repeating histidine residues retained the ability to induce IFN-γ secretion by ConA and PHA stimulated human blood mononuclear cells. Additionally, His or StrepII tagged polypeptides were able to mediate a therapeutic effect when tested *in vivo* (see Example 6, page 69, line 17 through page 71, line 24). These peptides have about 92% identity to those of SEQ ID NO: 2; thus, it is respectfully submitted that the as-filed specification enables polypeptides having at least 95% identity to those of SEQ ID NO: 2.

With respect to the issue raised as to fragments having the recited biological activity and/or those polypeptide fragments having at least 95% identity thereto, Applicants again respectfully submit that the as-filed specification teaches how one is to make and use these fragments. As indicated in the previous response, once given the amino acid sequence of SEQ ID NO: 2, the skilled person would be able to generate fragments and variants of SEQ ID NO: 2 using simple, well-known laboratory techniques (*e.g.* restriction cloning and/or error prone PCR), without undue burden or undue experimentation. Furthermore, one skilled in the art would have been able to test any fragments or variants so generated to identify polypeptides with interferon gamma-like activity, without undue burden. For example, the application discloses assays that can be used to identify suitable polypeptides on page 8:

> Interferon activity often measured as an anti-viral activity or antiproliferative activity on cancer cells. Examples of assays may be found in Schiller J.H, J Interferon Res 1986; 6(6):615-25, Gibson, U.E. et al., J Immunol Methods (1989) 20; 125(1-2): 105-13 and Chang et al., J. Biol. Chem. (2002) 277(9):7118-7126.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 6-8, and 51-62 are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description for fragments, "functional equivalents", or polypeptides having only 95% identity to the polypeptide of SEQ ID NO: 2. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan

that they had possession of the claimed invention. As noted above, the as-filed application discloses polypeptides having about 92% sequence identity to the claimed polypeptide (SEQ ID NO: 2). Thus, more than one example of a functional polypeptide that varies from SEQ ID NO: 2 in sequence is disclosed within the as-filed specification. Additionally, Applicants note that the currently amended claims are drawn to polypeptides that have, at most, three or four amino acid differences as compared to the full length of SEQ ID NO: 2. Applicants respectfully submit that such polypeptides (and fragments thereof) are adequately described within the as-filed specification. Particularly, the as-filed specification (at page 16, lines 19-29), discloses:

> ... [p]olypeptides in which one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code. Typical such substitutions are among Ala, Val, Leu and Ile; among Ser and Thr; among the acidic residues Asp and Glu; among Asn and Gln; among the basic residues Lys and Arg; or among the aromatic residues Phe and Tyr. Particularly preferred are variants in which several, i.e. between 5 and 10, 1 and 5, 1 and 3, 1 and 2 or just 1 amino acids are substituted, deleted or added in any combination. Especially preferred are silent substitutions, additions and deletions, which do not alter the properties and activities of the protein. Also especially preferred in this regard are conservative substitutions.

Thus, it is respectfully submitted that the as-filed specification provides adequate written description for the claimed polypeptides and fragments thereof and reconsideration and withdrawal of the rejection is respectfully requested.

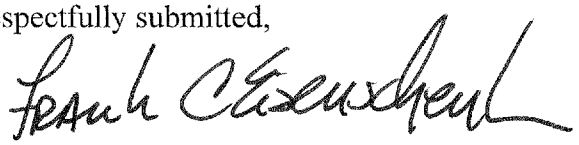
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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FCE/sl
Attachments: Office Action dated April 20, 2007 for Serial No. 10/872,859
Office Action dated November 2, 2007 for Serial No. 10/872,859

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/872,859	06/21/2004	Richard Joseph Fagan	674582-2003	4258

20999 7590 04/20/2007
FROMMER LAWRENCE & HAUG
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NEW YORK, NY 10151

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)
	10/872,859	FAGAN ET AL.
	Examiner	Art Unit
	Bruce D. Hissong, Ph.D.	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *18-30,32-45 and 49-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,31 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/18/05, 10/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence comparisons 1-5*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-17, 31, and 46-48, in the reply filed on 1/29/2007 is acknowledged.

2. Claims 1-59 are currently pending. Claims 18-30, 32-45, and 49-59 are withdrawn as non-elected subject matter, while claims 1-17, 31, and 46-48 are the subject of this office action.

Information Disclosure Statement

1. The information disclosure statement received on 4/18/2005 has been considered by the Examiner.

2. The information disclosure statement received on 10/12/2006 has been considered by the Examiner.

Drawings

The drawings submitted on 6/21/2004 are objected to because the text of some figures is too small and cannot be easily read. For example, the text in Figures 1 and 2, as well as the labeling of the vectors of Figures 5-10 is very small. Furthermore, some text of Figure 1 is hard to read due to the dark background behind the text.

Specification

The specification contains sequence listings that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the instant application fails to comply with the requirements of 37 CFR 1.821 – 1.825. Specifically, the sequences disclosed in Figures 11-13, as well as the sequences appearing on

pages 61-62 (Tables II and III) are not accompanied by the required sequence identifiers. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 – 1.825), and identify all sequences by sequence identifier.

Claim Objections

1. The Examiner suggest the syntax of claim 1 can be improved by amending the claim to read "An isolated polypeptide, wherein said polypeptide:".

2. The Examiner suggests amending claim 1, part (ii), to recite "having one or more".

3. The Examiner suggests that the phrase "four helical bundle cytokine fold", which appears throughout the claims, be amended to recite "four helical bundle cytokine fold family".

4. Claims 31 and 46-48 are objected to for reciting non-elected subject matter. Due to Applicants' election of Group I, drawn to polypeptides, the recitation of other types of molecules such as nucleic acids represents a recitation of non-elected subject matter.

5. The Examiner suggests amending claim 46 to recite a pharmaceutical composition comprising a polypeptide according to claim 1.....and a pharmaceutically acceptable carrier.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a polypeptide comprising or consisting of the amino acid sequence recited in SEQ ID NO: 36, or fragments or functional equivalents thereof. The polypeptide of SEQ ID NO: 36, or fragments or functional equivalents thereof can exist in nature, and as written, the claims do not show the "hand of man" in the inventive process. Therefore, the claims are directed towards non-statutory subject

matter. This rejection can be overcome by amending the claims to recite "An isolated polypeptide.....".

2. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. The claims of the instant invention are drawn to a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 36, fragments thereof, or functional equivalents thereof.

The Applicants have putatively identified the protein of their invention, SEQ ID NO: 36 or INSP037, as a member of the four helical bundle cytokine class, and more specifically, a member of the four helical bundle cytokine fold, and specifically an interferon-gamma (IFN-γ)-like molecule (p. 7, lines 21-24). However, the instant application does not disclose the biological role of the claimed protein or its significance, and the basis that the polypeptide of the present invention is an IFN-γ-like molecule is not predictive of a use. The specification does not disclose any function or disease state associated with altered levels of the polypeptide of SEQ ID NO: 36, or of any fragment of functional equivalent. The Applicants have only based the function of the protein of the present invention on homology to other members of the four helical bundle cytokine fold family. Therefore, the specific function of this protein, or any fragment or functional equivalent, would be speculative and significant, further experimentation would be required of the skilled artisan to identify a dysfunction or disease that is associated with the polypeptide (SEQ ID NO: 36). There is no disclosure, for example, of any symptoms associated with a disease or function of this polypeptide.

The specification discloses that the protein of SEQ ID NO: 36 (INSP037) has sequence similarity to members of the four helical bundle cytokine family members (see Example 1 and Figure 1). Based on the structural similarity, the specification asserts that the newly disclosed SEQ ID NO: 36 has a similar activity. The assertion that the disclosed polypeptide has biological activities similar to known four helical bundle cytokine family members cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick *et al* (2000, *Trends in Biotech.* 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36).

Similarly, Bork (2000, *Genome Research* 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks *et al.* (1998, *Trends in Genetics* 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith *et al.* (1997, *Nature Biotechnology* 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, *Trends in Genetics* 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork *et al.* (1996, *Trends in Genetics* 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the polypeptide of SEQ ID NO: 36, wherein said polypeptide is only known to be homologous to members of the four helical bundle cytokine family. Thus, the instant claims are drawn to a polypeptide that has an undetermined function or biological significance. There is no actual and specific significance identified in the specification that can be attributed to the polypeptide of SEQ ID NO: 36, or any fragment or functional equivalent thereof. For this reason, the instant invention is incomplete. In the absence of knowledge of the biological significance of this protein, there is no immediately obvious patentable use for it. To employ the polypeptide of the instant invention in the identification of substances which bind to and/or mediate activity of the said polypeptide is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for

said INSP037/SEQ ID NO: 36 protein, the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

> The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966) in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:
>
> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."
>
> There is little doubt that, after complete characterization, this protein, and therefore, the claimed antibody, will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, the Applicants' claimed invention is incomplete.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

1. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility. Therefore, claims 1-17, 31, and 46-48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility, for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

2. Furthermore, even if claims 1-17, 31, and 46-48 possessed utility, they would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for a polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 36, does not reasonably provide enablement for any fragment of the polypeptide of SEQ ID NO: 36, or any "functional equivalent" of the polypeptide of SEQ ID NO: 36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a polypeptide comprising or consisting of the amino acid sequence as recited in SEQ ID NO: 36, and fragments or functional equivalents thereof. The specification teaches that this polypeptide is an "IFN-γ-like" protein of the four helical bundle cytokine fold family. The breadth of the claims is excessively broad, however, because the claims read on any fragment having an antigenic determinant in common with the polypeptide of SEQ ID NO: 36, or any polypeptide/peptide that is a "functional equivalent" of the polypeptide of SEQ ID NO: 36, or any polypeptide or fragment that is "homologous" to SEQ ID NO: 36, wherein said polypeptide possesses "secreted protein functio ", "four helical bundle cytokine function", or "IFN-γ-like function." However, the claims do not specify or require any specific function of the claimed polypeptide, or specify or define any degree of similarity/identity that would make a polypeptide "homologous" to the polypeptide of SEQ ID NO: 36. The specification only requires that the polypeptide, fragment, or functional equivalent possess "secreted protein function", "four helical bundle cytokine function", or be "IFN-γ-like". Furthermore, the specification, on page 13, lines 15-18, states that the term "polypeptide" includes any peptide or protein comprising two or more amino acids. There is no guidance in the specification that would teach one of ordinary skill in the art how to make a peptide of only two amino acids, or of any other length, that could function as a "functional equivalent" of the polypeptide of SEQ ID NO: 36. A skilled artisan would not be able to predict which fragments of the polypeptide of SEQ ID NO: 36 would retain "secreted protein function", "four helical bundle cytokine function", or "IFN-γ-like" biological activity, and similarly, would not be able to predict how to make all possible "functional equivalents" of SEQ ID NO: 36, or determine which polypeptides that are "homologous" to the polypeptide of SEQ ID NO: 36 without guidance from the specification or specific limitations in the claims reciting a particular function or percent identity/similarity, respectively.

The claims are also drawn to polypeptide fragments or functional equivalents with at least 80%, 90%, 95%, 98%, or 99% sequence identity to the polypeptide of SEQ ID NO: 36, and also to fragments having any antigenic determinant in common with a polypeptide of SEQ ID NO: 36, which consists of 8, 10, 12, 14, 16, 18, or 20 or more amino acids from the sequence of SEQ ID NO: 36. However, the specification provides no guidance or examples which teach how to make any polypeptide with less than 100% sequence identity to SEQ ID NO: 36 that is still an "IFN-γ-like" polypeptide. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle *et al* (Med. Clin. North Am., 2000, Vol. 84(3), p. 597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR – p. 597). Several mutations can cause cystic fibrosis, including the G551D mutation. In this mutation, a glycine replaces the aspartic acid at position 551, giving rise to the cystic fibrosis phenotype. In the most common cystic fibrosis mutation, Δ-F508, a single phenylalanine is deleted at position 508, giving rise to the cystic fibrosis phenotype. Thus, even the substitution or deletion of a single amino acid can have dramatic and *unpredictable* effects on the function of the protein. Thus, a person of ordinary skill in the art would require further, undue experimentation to make, and then use, all possible fragments having an antigen determinant in common with the polypeptide of SEQ ID NO: 36, or any "functional equivalent" of the polypeptide of SEQ ID NO: 36, or any polypeptide with at least 80%, 90%, 95%, 98%, or 99% sequence identity to the polypeptide of SEQ ID NO: 36.

In summary, due to the excessive breadth of the claims, which read on any "functional equivalent" or peptide fragment with an antigenic determinant in common with the polypeptide of SEQ ID NO: 36, the lack of guidance or examples in the specification that teach which of the many possible fragments or functional equivalents could be "IFN-γ-like", and the unpredictability inherent in the art regarding how to make and then use such fragments or functional equivalents or homologous polypeptides, a person of ordinary skill in the art would require further, undue experimentation in order to make and use any fragment, functional equivalent, or polypeptide with less than 100% identity to the polypeptide of SEQ ID NO: 36.

3. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims of the instant invention are drawn to a polypeptide fragment having one or more of "secreted protein function", "four helical bundle cytokine function", and "interferon gamma-like function", or a functional equivalent of the fragment or the polypeptide from which the fragment is derived. The breadth of the claims is excessive because the claims are drawn to polypeptide fragments having biological activities associated with *any* secreted protein or *any* four helical bundle cytokine. Because there are many secreted proteins having vastly differing biological activities, and also because the four helical bundle cytokine family encompasses several different cytokines with differing activities, the claims are drawn to fragments having an unreasonably number of potential biological activities. In addition, the claims are drawn to fragments having any "IFN-γ-like" function. Various biological activities of IFN-γ are known in the art, but the claims do not limit any particular activity, or limit the degree to which a given activity may by IFN-γ "like". The claims do not recite any specific function or activity, and therefore the breadth of the recited functions of the claimed fragments is excessive. A person of ordinary skill in the art would not be able to predict how to make, and then use, all possible fragments that could be derived from SEQ ID NO: 36, wherein said fragments possessed all possible "secreted protein functions", "four helical bundle cytokine functions", or all possible functions that are "IFN-γ like". Such a determination would require significant, further experimentation on the part of a skilled artisan, and therefore the specification is not enabling for all possible fragments possessing all possible "secreted protein" functions, "four helical bundle cytokine" functions, or all possible "IFN-γ-like" functions.

4. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim recites a vaccine composition comprising a polypeptide of claim 1. As stated above in the rejection under 35 U.S.C. 101, there is no disclosed utility for the polypeptide of SEQ ID NO: 36, or any fragment or functional equivalent thereof, nor is there any disclosed disease or condition that is mediated

by this polypeptide, or associated with altered function of expression of this polypeptide. Therefore, one of ordinary skill in the art would not know how to use a vaccine comprising the polypeptide of claim 1, or any fragment or functional equivalent thereof. The breadth of the claim is excessive because it reads on a vaccine for any condition or disorder, and a skilled artisan would not be able to predict which of the many possible diseases or conditions would benefit from administration of a vaccine comprising the polypeptide of claim 1. Because the specification does not provide guidance or examples which teach which diseases or conditions could benefit from vaccination with the claimed vaccine composition, one of ordinary skill in the art would therefore require further, undue experimentation in order to make and then use a vaccine comprising the polypeptide of the instant invention, or any fragment or functional equivalent thereof.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the polypeptide recited in SEQ ID NO: 36, as well as any fragment having an antigen determinant in common with the polypeptide of SEQ ID NO: 36, any functional equivalent of SEQ ID NO: 36, and polypeptides having less than 100% sequence identity to SEQ ID NO: 36. The claims do not require the fragments, functional equivalents, or polypeptides with less than 100% sequence identity to SEQ ID NO: 36 of the instant invention to have any specific biological activity, nor any particular structure other than being functionally equivalent, a fragment of, or homology to SEQ ID NO: 36. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence relatedness to the polypeptide of SEQ ID NO: 36. In the instant case, this genus has not been adequately described in the instant specification, which only provides adequate written description of the polypeptide defined by SEQ ID NO: 36.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the claimed peptides be fragments of SEQ ID NO: 36, functional equivalents of SEQ ID NO: 36, or have at least 80% sequence identity to SEQ ID NO: 36, and be "IFN-γ-like". There is no identification of any particular portion of SEQ ID NO: 36 that must be conserved in order to produce a fragment, functional equivalent, or a polypeptide with less than 100% identity to SEQ ID NO: 36 that is "IFN-γ-like", or any disclosure defining or describing "IFN-γ-like" molecules. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite a polypeptide that is a "functional equivalent" of the polypeptide of SEQ ID NO: 36. The metes and bounds of this phrase are not defined by the claims, which do not specify any particular function for the claimed "functional equivalent".

2. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite a polypeptide, or fragment thereof, that has "interferon gamma-like function". The metes and bounds of the term "interferon gamma-like" are not defined by the claim, and thus the term "interferon gamma-like", which could mean virtually anything, is indefinite.

3. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a functional equivalent that exhibits "significant" structural

homology with the polypeptide of SEQ ID NO: 36. The metes and bounds of the term "significant" have not been defined by the claim or the specification, which do not teach any degree of homology that would represent a "significant" homology.

4. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a polypeptide that is a functional equivalent according to part (iii) of claim 1 and is homologous to the sequence of SEQ ID NO: 36. The claim does not specify any specific degree or percent homology, and thus the metes and bounds of the term "homologous" are not defined by the claim or the specification. The claims also do not define what type of homology the claimed polypeptide must possess, such as structural homology, functional homology, or something else.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

1. Claims 1-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Penn *et al* US 2002/0048763A1). The claims of the instant invention are drawn to a polypeptide comprising or consisting of the sequence of SEQ ID NO: 36, or fragments thereof having an antigenic determinant in common with the polypeptide of SEQ ID NO: 36, or functional equivalents thereof.

Penn *et al* teaches a polypeptide with several regions of identity to the polypeptide of SEQ ID NO: 36 (see sequence comparison 1). Specifically, the amino acids 22-26, 28-33, 57-61 of the polypeptide disclosed by Penn *et al* are identical to amino acids 14-18, 20-25, 49-53 of SEQ ID NO: 36 of the instant application, respectively. These regions of identity represent

fragments with 100% identity to the polypeptide of SEQ ID NO: 36, and because they represent peptides of 4-5 amino acids, would be expected, in the absence of evidence to the contrary, to be antigenic fragments. Therefore, the polypeptide of Penn *et al* meets the limitation of claim 1 of the instant application. These peptide regions taught by Penn *et al* would also be at least 80%, 90%, 95%, 98%, or 99% identical to antigenic fragments of SEQ ID NO: 36, and thus Penn *et al* meets the limitations of claims 4-8. Also, because the metes and bounds of the limitation "homology" are not defined, the peptide regions taught by Penn *et al* would exhibit significant (i.e. 100%) structural homology to the polypeptide of SEQ ID NO: 36, thus meeting the limitations of claim 9. Furthermore, because the metes and bounds of "interferon gamma-like" and "homology" are not clear, the polypeptide of Penn *et al* could be considered to be homologous to the instant SEQ ID NO: 36, and in the absence of evidence to the contrary, would be expected to function as either a secreted protein, a member of the four helical bundle cytokine fold, or as an interferon gamma-like molecule, and thus Penn *et al* also meets the limitations of claims 2-3. Finally, it is not clear if the fragment of claims 10-17 consists of 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids, or if the fragment of claim 10 has an antigenic determinant in common with a polypeptide having 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids. Because the claim can be interpreted either way, the peptide regions taught by Penn *et al* meet the limitations of claims 10-17 because they are fragments having an antigenic determinant in common with a polypeptide consisting of 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids (SEQ ID NO: 36).

2. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Drmanac *et al* (US 2005/0196754A1). Claims 1-9 of the instant invention are drawn to a polypeptide, wherein said polypeptide can be a fragment having an antigenic determinant in common with the polypeptide of SEQ ID NO: 36. Claims 10-17 are further drawn to the fragment of claim 1, wherein the fragment consists of 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acid residues from the sequence of SEQ ID NO: 36. Claim 31 is drawn to the polypeptide of SEQ ID NO: 36 for use in therapy or diagnosis of disease, while claims 46-48 recite a pharmaceutical composition and a vaccine composition comprising the polypeptide of SEQ ID NO: 36, and the polypeptide of SEQ ID NO: 36 for use in treatment of various diseases.

Drmanac *et al* teaches a polypeptide with several regions of identity to the polypeptide of SEQ ID NO: 36 (see sequence comparison 2). Specifically, amino acids 127-136 of the

polypeptide disclosed by Drmanac *et al* are identical to amino acids 37-46 of SEQ ID NO: 36 of the instant application. This region represents a region of 100% identity to a fragment of SEQ ID NO: 36, spans 10 amino acids, and could be considered, in the absence of evidence to the contrary, to represent an antigen fragment. Thus, the disclosure of Drmanac *et al* meets the limitations of claims 1 and 10-12 of the instant application. Dramanac *et al* also discloses a peptide with 100% identity to a region of 12 amino acid residues of SEQ ID NO: 36 of the instant application (see sequence comparison 3), and thus meets the limitations of claims 1 and 10-13 of the instant application. These peptides regions taught by Drmanac *et al* would also be at least 80%, 90%, 95%, 98%, or 99% identical to an antigenic fragment of SEQ ID NO: 36, and thus Drmanac *et al* meets the limitations of claims 4-8. Also, because the metes and bounds of the limitation "significant structural homology" are not defined, the peptide region taught by Drmanac *et al* would exhibit significant (i.e. 100%) structural homology to the polypeptide of SEQ ID NO: 36, thus meeting the limitations of claim 9. Furthermore, because the metes and bounds of "interferon gamma-like" and "homology" are not clear, the polypeptide of Drmanac *et al* could be considered to be homologous to the instant SEQ ID NO: 36, and in the absence of evidence to the contrary, would be expected to function as either a secreted protein, a member of the four helical bundle cytokine fold, or as an interferon gamma-like molecule, and thus Drmanac *et al* also meets the limitations of claims 2-3. Additionally, it is not clear if the fragment of claims 10-17 consists of 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids, or if the fragment of claim 10 has an antigenic determinant in common with a polypeptide having 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids. Because the claim can be interpreted either way, the peptide regions taught by Penn *et al* meet the limitations of claims 10-17 because they are fragments having an antigenic determinant in common with a polypeptide consisting of 7, 8, 10, 12, 14, 16, 18, or 20 or more amino acids (SEQ ID NO: 36). Finally, Drmanac discloses pharmaceutical and vaccine compositions comprising the disclosed polypeptide (paragraphs 0014 and 0275), and treatment of various diseases, including multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis, by administration of the disclosed polypeptide (paragraphs 0025 and 0201). Therefore, the disclosure of Drmanac et al meets the limitations of claims 31 and 46-48 of the instant application.

3. Claims 1-17, 31, and 46-48 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The instant application, drawn to the

polypeptide of SEQ ID NO: 36, or fragments or functional equivalents thereof, and copending application 10/558,800 drawn to the polypeptide of SEQ ID NO: 2, which is 100% identical to SEQ ID NO: 36 of the instant application (see sequence comparison 4), recite identical subject matter. However, inventors Boschert and Chvatchko of the copending application 10/558,800 are not named as inventors of the instant application, which claims identical subject matter. Therefore, it is not clear that the inventors of the instant application did indeed invent the claimed subject matter of the instant application, or if inventors Boschert and Chvatchko invented the claimed subject matter of the instant invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-17, 31, and 46-48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43 and 64-65 of copending Application No. 10/558,800. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 43 and 64-65 of the '800 application are drawn to a polypeptide that is 100% identical to SEQ ID NO: 36 of the instant application (see sequence comparison 4), or fragments or functional equivalents thereof, as well as pharmaceutical and vaccine compositions, and uses for therapy or diagnosis of disease. Therefore, because both applications are drawn to identical polypeptides, or fragments derived

from identical polypeptides, it would be obvious to a person of ordinary skill in the art that the subject matter of the '800 application is encompassed by the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

2. Claims 1-17, 31, and 46-48 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10, 21, and 32-34 of copending Application No. 10/600,790. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The instant application is drawn to a polypeptide of the sequence defined by SEQ ID NO: 36, and fragments or functional equivalents thereof, as well as polypeptides having at least 80%, 90%, 95%, 98%, or 99% identity to the polypeptide of SEQ ID NO: 36. Claims 1-10, 21, and 32-34 of copending Application 10/600,790 recite a polypeptide of the sequence defined by SEQ ID NO: 2, and fragments or functional equivalents thereof, as well as polypeptides having at least 80%, 90%, 95%, 98%, or 99% identity to the polypeptide of SEQ ID NO: 2, pharmaceutical and vaccine compositions, and use of the polypeptide for treatment or diagnosis of disease. Because SEQ ID NO: 36 of the instant application is 100% identical to SEQ ID NO: 2 of copending Application 10/600,790 (see sequence comparison 5), the two application recite identical subject matter.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The Examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/872,859	06/21/2004	Richard Joseph Fagan	C&R-118	4258

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
11/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/872,859	FAGAN ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133) Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10-17,47 and 61-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 10-17, 47, 61-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/23/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The Applicants' response to the office action mailed on 4/24/2007, including arguments/remarks and amended claims, specification, and drawings, was received on 8/20/2006 and has been entered into the record.

2. In the response received on 8/20/2007, the Applicants cancelled claims 2-9, 18-46, and 48-59, and added new claims 60-81. Therefore, claims 1, 10-17, 47, and 60-81 are currently pending and are the subject of this office action.

Information Disclosure Statement

The information disclosure statement received on 4/23/2007 has been considered by the Examiner.

Drawings

The drawings submitted on 8/20/2007 *remain objected* to because Figures 1 and 5-10 contains text which has been cut off at the end of the page.

Specification

Objection to the specification regarding sequence listings without a sequence identifier, as set froth on pages 2-3 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the specification to provide sequence identifiers for recited sequences.

Claim Objections

1. Objection to claim 1, as set forth in objections 1 and 2 on page 3 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' making all necessary amendments to the claim to overcome these objections.

2. Objection to the claims regarding the term "four helical bundle cytokine fold", as set forth on page 3 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to delete the term from the claims.

3. The Examiner suggests amending claim 10 to recite "wherein said fragment consists of 7 or more consecutive amino acids" in order to be consistent with the language of the other claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Rejection of claims 1, 10-17, and 47 under 35 USC § 101, as being directed to non-statutory subject matter, as set forth on pages 3-4 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the claims to recite "An isolated polypeptide".

2. Rejection of claims 1, 10-17, and 47 under 35 USC § 101, as not supported by a specific, substantial and credible asserted utility, or a well established utility, as set forth on pages 4-6 of the office action mailed on 4/24/2007, is *withdrawn*. In the response received on 8/20/2007, the Applicants argue that the polypeptide of the instant invention, INSP037/SEQ ID NO: 2, was disclosed in the specification of co-pending application 10/600,790 as exhibiting the ability to stimulate interferon (IFN)-γ production *in vitro* and *in vivo*, and thus possesses a specific, substantial and credible asserted utility.

These arguments have been fully considered and are persuasive.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejections withdrawn

1. Rejection of claims 1, 10-17, and 47 under 35 USC § 112, first paragraph, regarding lack of enablement because the claimed invention is not supported by a specific, substantial and credible asserted utility, or a well-established utility, as set forth on page 6 of the office action mailed on 4/24/2007, is *withdrawn*. In the response to the Applicant's arguments, the rejection under 35 USC 101 has been withdrawn (see above), along with the accompanying rejection under 35 USC 112, first paragraph.

2. Rejection of claims 1, 10-17, and 47 under 35 USC § 112, first paragraph, regarding lack of enablement for a polypeptide having one or more of "secreted protein function", "four helical bundle cytokine function" and "interferon gamma-like function", as set forth on page 9 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the claims to delete these limitations.

3. Rejection of claim 47 under 35 USC § 112, first paragraph, regarding lack of enablement for a vaccine composition comprising the INSP037/SEQ ID NO: 2 polypeptide, as set forth on pages 9-10 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' arguments that the polypeptide of SEQ ID NO: 2 exhibits the ability to stimulate IFN-γ production, and thus has utility regarding vaccine compositions, as IFNs are known to be potent vaccine adjuvants.

Rejections maintained

4. Claims 1, 10-17, 47 *remain rejected*, and new claims 61-80 are also rejected under 35 USC § 112, first paragraph, regarding lack of enablement for a polypeptide consisting of a fragment of SEQ ID NO: 2, wherein said fragment exhibits antiviral or antiproliferative activity, as set forth on pages 7-8 of the office action mailed on 4/24/2007.

In the response received on 8/20/2007, the Applicants argue that the specification is enabling for the claims as currently amended because the claims have been amended to delete limitation "functional equivalent", and the specification provides guidance for fragments of SEQ ID NO: 2. Specifically, the Applicants argue that the specification teaches the amino acid sequence of SEQ ID NO: 2, as well as suitable assays to identify polypeptides having antiviral or antiproliferative activity. Furthermore, muteins, variants, and mutants of IFN-γ polypeptides are known in the art, and therefore it would require

only routine experimentation for a skilled artisan to make and use fragments of SEQ ID NO: 2 having antiviral or antiproliferative activity.

These arguments have been fully considered and are not persuasive. The specification does not teach or provide examples of any fragments of SEQ ID NO: 2, such as fragments having only 7 amino acids, having any biological activity, whether "IFN-γ-like" or otherwise. Although the art does teach various muteins, variants, and mutants of IFN-γ, these variants are generally full-length variants or mutants and not 7-20 amino acid peptides. The guidance of the specification and the art also does not allow one to predict which of the many possible 7-20 amino acid fragments of SEQ ID NO: 2 would be expected to exhibit any IFN-γ-like activity, such as antiviral or antiproliferative activity. Furthermore, it is also noted that in response to the rejections under 35 USC 102 (see below), the art taught peptide fragments identical to regions of SEQ ID NO: 2. However, the Applicants have asserted that these fragments would not be expected to exhibit antiviral or antiproliferative activity. The specification does not allow one of skill in the art, therefore, to discriminate between peptides of SEQ ID NO: 2 which do exhibit antiviral or antiproliferative activity, and those that do not because the specification does not teach which regions of SEQ ID NO: 2 would be expected to exhibit these activities. Therefore one of ordinary skill in the art would require further, undue experimentation in order to practice the claimed invention in a manner commensurate with the full scope of the claims.

Rejections necessitated by amendment

5. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2 fused to a compound or a heterologous amino acid sequence, does not reasonably provide enablement a vaccine composition comprising the polypeptide of SEQ ID NO: 2 fused to a compound or a heterologous amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 47 reads on a vaccine composition comprising polypeptides fused to all possible compounds or heterologous amino acid sequences. Although fusion to various compounds and heterologous sequences is known in the art, the specification does not provide guidance or examples showing which compounds and heterologous amino acid sequences may be fused to the claimed polypeptide while still being used as a vaccine component. A person of ordinary skill in the art would not be able to predict the effect of immunogenic or adjuvant activity of fusing all possible compounds or polypeptide sequences to that of SEQ ID NO: 2. For example, would SEQ ID NO: 2, or a fragment of

SEQ ID NO: 2 consisting of 7 amino acids, fused to a heterologous amino acid sequence derived from an insect protein still retain the desired immunogenicity or adjuvanticity in order to be useful in a vaccine compositions? Thus, although compounds and heterologous amino acid sequences useful for fusion to polypeptides are known in the art, the effect of fusion of these compounds and heterologous sequences to a protein of a vaccine composition is not predictable, and a person of ordinary skill in the art would therefore require further, undue experimentation in order to determine which of the many possible compounds and/or heterologous amino acid sequences can be used in the context of a vaccine composition.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejections maintained

1. Claims 1, 10-17, 47 *remain rejected*, and new claims 61-80 are also rejected under 35 USC § 112, first paragraph, regarding lack of written description for the genus of polypeptides consisting of a fragment of SEQ ID NO: 2, wherein said fragment exhibits antiviral or antiproliferative activity, as set forth on pages 10-11 of the office action mailed on 4/24/2007.

In the response received on 8/20/2007, the Applicants argue that the claims have now been amended to recite isolated polypeptides which have antiviral or antiproliferative activity on cancer cells, and thus have been adequately described by reciting functional limitations.

These arguments have been fully considered and are not persuasive. As set forth above in the rejection under 35 USC 112, first paragraph, regarding lack of enablement for fragments of SEQ ID NO: 2, the claims read on any 7-20 amino acid sequence of SEQ ID NO: 2 that exhibits antiviral or antiproliferative activity. However, it is noted that the instant specification teaches that the claimed polypeptide of SEQ ID NO: 2 is "IFN-γ like", and while the specification predicts that the claimed polypeptide exhibits antiviral or antiproliferative activity, there is no disclosure indicating that it actually does so. Furthermore, even if the claimed polypeptide does indeed exhibit antiviral or antiproliferative activity, there is no disclosure of any domains, regions, or amino acid sequences that must be conserved in a fragment of SEQ ID NO: 2 in order to maintain antiviral or antiproliferative activity. It is also noted that in response to the rejections under 35 USC 102 (see below), the art taught peptide fragments identical to regions of SEQ ID NO: 2. However, the Applicants have asserted that these fragments would not be expected to exhibit antiviral or antiproliferative activity. The specification does not allow one of skill in the art, therefore, to discriminate between peptides of SEQ ID NO: 2 which do exhibit antiviral or

antiproliferative activity, and those that do not because the specification does not describe which peptide regions of SEQ ID NO: 2 would be expected to exhibit these activities. Thus, the specification does not adequately describe the genus of fragments of SEQ ID NO: 2 that would be expected to exhibit antiviral or antiproliferative activity.

Rejections necessitated by amendment

2. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a vaccine composition comprising the polypeptide of SEQ ID NO: 2 fused to a compound or heterologous amino acid sequence. The claims do not require either the compound or the heterologous amino acid sequences of the instant invention to have any biological activity, nor any particular structure. While the art teaches polypeptide fusion to various compounds and heterologous amino acid sequences, this by itself is insufficient to described the claimed genus of compounds or heterologous amino acid sequences capable of being fused to the polypeptide of SEQ ID NO: 2 while retaining the ability of the SEQ ID NO: 2 polypeptide to function in a vaccine as either an immunogen or an adjuvant.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that any compound or heterologous amino acid sequence, of any type or structure, be fused to the claimed polypeptide comprising the claimed vaccine composition. There is no identification of any particular heterologous amino acid sequence or any compound that can be used while maintaining immunogenicity or adjuvanticity. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

3. Claims 1, 10-17, 47, and 61-80 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims of the instant invention are also drawn to an isolated polypeptide comprising the "mature form" of the polypeptide of SEQ ID NO: 2. However, the specification does not provide a description of what residues of SEQ ID NO: 1 represents the "mature" form, or any pre- or pro-form of SEQ ID NO: 2. There is no description of any residues of SEQ ID NO: 2 which are not considered to be residues of a "mature" form of SEQ ID NO: 1, nor any disclosure of which residues must be conserved in order to designate a polypeptide as a mature form of SEQ ID NO: 2. Accordingly, the genus of polypeptides representing the "mature form" of SEQ ID NO: 2 has not been adequately described by the specification.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the claimed polypeptide be the "mature form" of SEQ ID NO: 2. There is no identification of any particular amino acid sequence that is a "mature form" of SEQ ID NO: 2 Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

1. Rejection of claims 1, 10-17, and 47 under 35 USC § 112, second paragraph, as being indefinite regarding the terms "functional equivalent" and "interferon gamma-like function", as set forth on page 11 of the prior office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the claims to delete these terms.

Rejection necessitated by amendment

2. Claims 1, 10-17, 47, and 61-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. The claims are drawn to an isolated polypeptide that "is the mature form of the polypeptide of SEQ ID NO: 2". The specification teaches the amino acid sequence of SEQ ID NO: 2, but does not teach if this is the "mature" form of the polypeptide, and if not, what constitutes the "mature" form of SEQ ID NO: 2. Furthermore, the specification teaches that the "mature" form the polypeptide lacks the pre-, pro- or prepro- sequences, and that the "leader sequences" are cleaved; however, the identity of these pre-, pro-, prepro-, and leader sequences is not clear, and thus a skilled artisan would not know what sequence(s) represents the "mature" form of the polypeptide. For these reasons, the metes and bounds of the term "mature form of the polypeptide of SEQ ID NO: 2" cannot be determined.

3. Claim 47 recites the limitation "said isolated polypeptide" in part (iv) of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

1. Rejection of claims 1 and 10-17 under 35 USC § 102(e) as being anticipated by Penn *et al* (US 20020048763A1), as set forth on pages 12-13 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the claims to recite a polypeptide of SEQ ID NO: 2 having antiviral or antiproliferative activity on cancer cells. The Applicants argue that the fragments of the polypeptide of Penn *et al* having identity to SEQ ID NO: 2 (previously SEQ ID NO: 36) would not be expected to exhibit antiviral or antiproliferative activity on cancer cells.

This argument has been fully considered and is persuasive in view that it would be difficult to make a *prima facie* case that the fragments of Penn *et al* would indeed have antiviral activity or antiproliferative activity. It is also noted that although this rejection is withdrawn in response to the

Applicants' arguments that this reference does not teach fragments with antiviral or antiproliferative activity, the scope of enablement and written description rejections (see above) are warranted.

2. Rejection of claims 1, 10-17, and 47 under 35 USC § 102(e) as being anticipated by Drmanac *et al* (US 20050196754A1), as set forth on pages 13-14 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' amendments to the claims to recite a polypeptide of SEQ ID NO: 2 having antiviral or antiproliferative activity on cancer cells. The Applicants argue that the fragments of the polypeptide of Drmanac *et al* having identity to SEQ ID NO: 2 (previously SEQ ID NO: 36) would not be expected to exhibit antiviral or antiproliferative activity on cancer cells.

This argument has been fully considered and is persuasive because it would be difficult to make a *prima facie* case that the fragments of Drmanac *et al* would indeed have antiviral activity or antiproliferative activity. It is also noted that although this rejection is withdrawn in response to the Applicants' arguments that this reference does not teach fragments with antiviral or antiproliferative activity, the scope of enablement and written description rejections (see above) are warranted.

3. Rejection of claims 1, 10-17, and 47 under 35 USC § 102(f) as set forth on pages 14-15 of the office action mailed on 4/24/2007, is *withdrawn* in response to Applicants' cancellation of claims 1-43 of Application No. 10/558,800, and submission of new claims drawn to methods of using a polypeptide of SEQ ID NO: 2.

Double Patenting

Nonstatutory double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided

the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejections withdrawn

1. Rejection of claims 1, 10-17, and 47 on the grounds of nonstatutory obviousness-type double patenting, as being unpatentable over claims 43 and 64-65 of copending Application No. 10/558,800, as set forth on pages 15-16 of the office action mailed on 4/24/2007, is *withdrawn* in response to the cancellation of claims 43 and 64-65 of the '800 application.

Rejections necessitated by amendment

2. Claims 1, 10-17, 47, and 61-80 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-8, and 51-62 of copending Application No. 10/600,790. Although the conflicting claims are not identical due to the recitation of the limitations including fusion to heterologous amino acid sequences and compounds in the instant application, they are not patentably distinct from each other. In the instant case, both applications are drawn to identical polypeptides, as set forth on pages 15-16 of the previous office action, as well as fragments of said polypeptides having antiviral or antiproliferative effects on cancer cells. Although the claims of the '790 application do not recite fragments consisting of 7, 8, 10, 12, 14, 16, 18, or 20 amino acids, the specification of the '790 application teaches that fragments of these sizes are preferable (p. 17, lines 20-25). Furthermore, the specification of the '790 application (p. 38, lines 15-19 and p. 43, lines 2-10) teaches that the polypeptide of the invention can be used in a vaccine composition. Therefore, although the claims of the '790 application do not recite fragments of specific sizes or a vaccine composition comprising the polypeptide of the invention, it would be obvious to a person of skill in the art to create such fragments and vaccine compositions because the specification of the '790 teaches such embodiements. Because both applications therefore are drawn to the same polypeptides and fragments which would overlap in scope, as well as compositions which overlap in scope, the claims of the instant application are obvious in view of the claims of the '790 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Statutory double patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Rejection of claims 1, 10-17, and 47 under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 6-8 of copending Application No. 10/600,790, as set forth on page 16 of the office action mailed on 4/24/2007, is withdrawn in response to Applicants' amendments to the instant claims to recite polypeptides of SEQ ID NO: 2 fused to a heterologous amino acid sequence or a compound. The Applicants argue that the instant claims are not identical to those of the '790 application.

These arguments have been fully considered and are persuasive.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Robert S. Landsman/
Primary Examiner, Art Unit 1647